

June 12, 2003

David B. Bower, Ph.D.
Product Risk Manager
R.T. Vanderbilt Company, Inc.
P.O. Box 5150
Norwalk, CT 06856

Dear Dr. Bower:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 2-H-Benzimidazole-2-thione, 1,3-dihydro-4 (or 5)-methyl-, Zinc Salt (2:1) posted on the ChemRTK HPV Challenge Program Web site on January 31, 2003. I commend The R.T. Vanderbilt Company, Inc. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The R.T. Vanderbilt Company, Inc. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission: Zinc Mercaptotoluimidazole

Summary of EPA Comments

The sponsor, the R. T. Vanderbilt Company, Inc., submitted a test plan and robust summaries to EPA for Zinc Mercaptotoluimidazole (CAS No. 61617-00-3) dated January 02, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 31, 2003.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. Adequate data are available for all endpoints except partition coefficient and water solubility for the purposes of the HPV Challenge Program. The submitter needs to measure the partition coefficient and to determine whether the methodology used to measure water solubility was appropriate.
2. Health Effects. EPA agrees with the proposal to conduct a combined repeated-dose, reproduction and developmental toxicity screening test. In addition, the submitter needs to conduct an *in vitro* mammalian chromosomal aberrations test and address deficiencies in the robust summaries.
3. Ecological Effects. EPA agrees with the plan to conduct testing for the fish, invertebrate, and algal endpoints. In addition, a chronic toxicity study in daphnia is necessary if the measured log K_{ow} is determined to be ≥ 4.2 .

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Zinc Mercaptotoluimidazole Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

Adequate data are available for all endpoints except partition coefficient and water solubility for the purposes of the HPV Challenge Program.

Partition coefficient. The submitter states that an estimated value is adequate for this endpoint. EPA disagrees. The EPIWIN software was not designed to estimate values for organometallic compounds. The submitter needs to determine a measured value using OECD TG 107/117.

Water solubility. The submitter reports a measured value of 32 mg/L conducted according to OECD TG 105 and GLP. It is unclear whether the study was conducted by the shake flask or the HPLC method. According to the guideline, the shake flask method should not be used if the water solubility is expected to be less than 0.01 g/L. In that region, the shake flask method may provide a higher value than the true solubility. Furthermore, the zinc derivative would be expected to be less soluble than the corresponding thiol, for which EPIWIN estimated a solubility of 3 mg/L. The submitter needs to clarify the methodology used and determine whether it was appropriate.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

Adequate data are available for all environmental fate endpoints for the purposes of the HPV Challenge Program.

Stability in water. The test plan states that this endpoint will be met using calculated data. However, HYDROWIN cannot estimate hydrolysis rate constants for metal salts. Therefore, the submitter should refer in the test plan to a “technical discussion” and add a discussion on the lack of hydrolyzable functional groups to the robust summary.

Biodegradation. The submitter needs to correct the statement in the test plan summary that a ready biodegradation study is planned, which conflicts with the test plan.

Fugacity. The submitter needs to provide input parameters in the robust summary.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for the acute toxicity and gene mutation endpoints. EPA agrees with the submitter's proposal to conduct a combined repeated-dose, reproduction and developmental toxicity screening test following OECD TG 422. The submitter needs to address deficiencies in the robust summaries.

Genetic toxicity (chromosomal aberrations). No data were submitted and no testing is proposed. EPA disagrees with the view that bacterial mutation studies serve as an “initial screen” for chromosomal aberration potential. The submitter needs to conduct an *in vitro* mammalian chromosomal aberrations test following OECD TG 473.

Ecological Effects (fish, invertebrates, and algae)

EPA agrees with the submitter's plan to conduct testing for the fish, invertebrate, and algal endpoints. The tests should be conducted according to OECD TG's 201, 202, and 203, using mean measured concentrations. It would be helpful in interpreting the test results if concentration monitoring included the measurement of the equilibrium concentration of zinc ion and/or toluimidazolethiolate ion.

Chronic toxicity. If the measured log K_{ow} from the recommended partition coefficient study is ≥ 4.2 , chronic effects in aquatic organisms may occur. Therefore, additional testing to obtain chronic toxicity data on aquatic invertebrates is needed because this class of chemical may show both acute and chronic effects.

Specific Comments on the Robust Summaries

Health Effects

Acute toxicity. The omitted information for the acute oral toxicity study included length of the observation period and a range or 95% confidence interval for the LD₅₀. There is a discrepancy or a typographical error in the supporting data from the acute inhalation toxicity study: the LC₅₀ (4 hr) was reported as > 2.03 mg/l, but the tested dose was 2.13 mg/l. Also, the OECD test guideline number for the acute inhalation toxicity study should be 403 instead of **073**.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.